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ORIGINAL ARTICLE

Morbidity of central compartment dissection for differentiated thyroid carcinoma of the follicular epithelium

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Central compartment dissection;
Thyroid carcinoma;
Lymph node metastasis;
Recurrent laryngeal nerve paralysis;
Hypoparathyroidism

Summary
Objectives: To study the morbidity of central compartment dissection in differentiated thyroid carcinoma of the follicular epithelium.
Material and method: A retrospective study of 83 patients (61 patients operated by total thyroidectomy and 22 patients operated by total thyroidectomy and central dissection) was performed. Postoperative serum calcium and laryngeal mobility were studied and statistically compared (Chi^2 test, Fisher's exact test).
Results: No significant difference was observed between the two groups in terms of the incidence of recurrent laryngeal nerve paralysis or permanent hypoparathyroidism. In contrast, transient hypoparathyroidism was more frequent among patients undergoing thyroidectomy associated with central dissection ($P = 0.02$).
Conclusion: Central compartment dissection associated with total thyroidectomy does not increase the risk of recurrent laryngeal nerve paralysis or permanent hypoparathyroidism, but is responsible for an increased rate of transient hypoparathyroidism.

Introduction

Differentiated thyroid carcinoma of the follicular epithelium is the most common endocrine cancer (5000 new cases per year in France) [1]. The incidence of this tumour has increased as a result of earlier diagnosis and changing clinical practice (extension of the indications for thyroid surgery, improved histological diagnosis) [1].

French, European and Americans guidelines on thyroid carcinoma are relatively consensual, except for certain aspects, especially the indications for prophylactic central compartment dissection for stage T1 or T2 papillary carcinoma [1—4].

This study was designed to evaluate the morbidity of central compartment dissection in order to clarify the controversial indications for this type of lymph node dissection.

Population and method

This retrospective study was based on an 11-year period (January 1998 to November 2009).

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Population

Eighty-three patients (46 women and 37 men) with a mean age of 51 years (standard deviation: 14.1) were included in this study.

Method

Inclusion criteria were as follows:

- patients of any age and gender;
- patients with thyroid carcinoma of the follicular epithelium;
- patients operated by total thyroidectomy;
- patients operated by total thyroidectomy associated with central compartment (level VI) lymph node dissection.

Patients treated by subtotal thyroidectomy or loboisthmectomy were excluded from the study.

Preoperative assessment for all patients consisted of:

- thyroid hormone assays: TSH, T3, T4;
- thyroid ultrasound.

Some patients were assessed by:

- contrast-enhanced neck and chest CT scan;
- ultrasound-guided fine-needle aspiration cytology of suspicious nodules, essentially after 2001.

All patients were operated by total thyroidectomy with frozen section histological examination and all operations were performed by experienced surgeons. The lymph node surgical strategy was decided on the basis of imaging findings and frozen section histological examination results.

Surgical modalities

All patients were operated by total thyroidectomy via a small neck incision. Sternotomy was never required. Thyroidectomy was always performed by capsular dissection, with identification and anatomical preservation of the recurrent laryngeal nerve. In the event of accidental parathyroidectomy, the parathyroid glands concerned were reimplanted in the sternocleidomastoid muscle in two or three sites after fragmentation of the glands.

Central compartment or level VI lymph node dissection consisted of resection of all adipose connective tissue between the hyoid bone superiorly, the brachiocephalic vein, the jugular and carotid vascular fascia laterally, the oesophagus posteriorly, and the prelaryngeal muscles anteriorly, with preservation of the recurrent laryngeal nerves and parathyroid glands.

Laryngoscopic surveillance

Indirect laryngoscopy was systematically performed postoperatively before the patient's discharge from hospital and again on the thirtieth postoperative day, even in the absence of voice disorders.

Persistent hoarseness related to recurrent laryngeal nerve paralysis after 1 year was considered to be permanent. All patients with recurrent laryngeal nerve paralysis were treated by early speech therapy.

Cases of preoperative recurrent laryngeal nerve paralysis or resulting from sacrifice of the recurrent laryngeal nerve for oncological reasons were classified as sequelae rather than complications.

Surveillance of serum calcium

Hypoparathyroidism was considered to be present whenever calcium and vitamin D replacement therapy was necessary to obtain corrected serum calcium higher than 2 mmol/L. Hypoparathyroidism was considered to be permanent when calcium and vitamin D replacement therapy was necessary for more than 1 year. Corrected serum calcium assays were performed on D1, D2, D3, and D10 and specific follow-up was then instituted in the presence of any abnormalities.

Statistical analysis

Statistical analysis was performed by means of Chi^2 test or Fisher's exact text, as appropriate. *P* values less than 0.05 were considered significant.

Results

Tumour characteristics

Seventy-six patients (91.6%) had a papillary carcinoma and seven patients (8.4%) had a follicular carcinoma. Patients were classified into four stages according to the UICC classification:

- 45 patients (54.2% of cases) were classified as stage I;
- six patients (7.2% of cases) were classified as stage II;
- 10 patients (12.1% of cases) were classified as stage III;
- 22 patients (26.5% of cases) were classified as stage IV.

Sixty-one patients (73.5%) underwent level VI lymph node dissection.

A two-stage surgical strategy (completion thyroidectomy) was necessary for 18 patients (21.7% of cases), but no secondary recurrent laryngeal dissection was performed. Thirty-six patients (43.4% of cases) had a papillary microcarcinoma and 29 patients (35% of cases) had a multifocal cancer. Twenty-seven patients (44% of cases) presented signs of lymph node invasion. Two (16.7%) of the 12 patients with a microcarcinoma less than 5 mm in diameter presented level VI lymphadenopathy, while 14 (58.3%) of the 24 patients with a microcarcinoma more than 5 mm in diameter presented level VI lymphadenopathy. Level VI lymph node dissection was not performed in nine of these 36 patients.

Postoperative recurrent laryngeal nerve paralysis

Nine patients (10.8%) presented transient recurrent laryngeal nerve paralysis and three patients (3.6%) presented permanent recurrent laryngeal nerve paralysis. One patient

Table 1 Postoperative complications.

	Number	Percentage
Transient RLNP	9	10.8
Permanent RLNP	3	3.6
Transient hypoparathyroidism	28	33.7
Permanent hypoparathyroidism	6	7.2
Haematoma	1	1.2
Operative site infection	2	2.4
Keloid scar	2	2.4
Bilateral RLNP	1	1.2
Pneumonia	1	1.2
Death due to postoperative cardiorespiratory arrest (massive pulmonary embolism)	1	1.2

RLNP: recurrent laryngeal nerve paralysis

Table 2 Comparison of complications between total thyroidectomy (TT) and thyroidectomy with level VI lymph node dissection (TT + VI group).

	TT (group A)	TT + VI (group B)	*P*
Transient RLNP	3	6	0.693[b]
Permanent RLNP	1	2	0.669[b]
Transient hypoparathyroidism	3	25	0.02[a]
Permanent hypoparathyroidism	2	4	0.653[b]

RLNP: recurrent laryngeal nerve paralysis
[a] Chi^2 test.
[b] Fisher's exact test.

presented bilateral recurrent laryngeal nerve paralysis, which was only transient on one side. Tracheotomy was not required.

Postoperative hypoparathyroidism

Twenty-eight patients (33.7%) presented transient hypoparathyroidism and six patients (7.2%) presented permanent hypoparathyroidism.

Other complications

Other complications are listed in Table 1.

Statistical analysis

Patients were divided into two groups:

- group A: total thyroidectomy only (22 patients);
- group B: total thyroidectomy with central compartment dissection (61 patients).

No statistically significant difference was observed between the two groups in terms of recurrent laryngeal nerve paralysis (transient or permanent) or permanent hypoparathyroidism. In contrast, transient hypoparathyroidism was significantly more frequent in group B ($P = 0.02$) (Table 2).

Discussion

Recurrent laryngeal nerve paralysis

According to the literature, the incidence of transient recurrent laryngeal nerve paralysis after total thyroidectomy for thyroid cancer is 1 to 10%. In 1 to 5.6% of cases, recurrent laryngeal nerve paralysis is permanent [1,5,6]. Our results, based on a relatively small series, confirm these data. Furthermore, as demonstrated by Chisholm et al. [5], level VI lymph node dissection associated with total thyroidectomy does not appear to have any impact on the incidence of recurrent laryngeal nerve paralysis.

Transient hypoparathyroidism

The incidence of transient hypoparathyroidism varies considerably from one series to another, ranging from 3 to 83% [1,5,7,8].

The results of the present study (33.7% of transient hypoparathyroidism) are also consistent with those reported in the literature, situated in the middle of the range. Central compartment (level VI) lymph node dissection was associated with a higher rate of transient hypoparathyroidism than that observed after total thyroidectomy alone ($P = 0.02$), confirming the data reported by Chisholm et al. [5].

This transient hypoparathyroidism can be essentially explained by extension of thyroid dissection causing microscopic vascular lesions altering the quality of the blood supply to the parathyroid glands [1,9,10], rather than accidental parathyroidectomy, which does not appear to be more frequent in the case of level VI lymph node dissection and which, moreover, generally does not have any impact on serum calcium [11].

Permanent hypoparathyroidism

The incidence of permanent hypoparathyroidism after total thyroidectomy (for thyroid cancer or other indications) reported in the literature ranges from 0 to 29% of cases [1,5,7,8]. The findings in our series were consistent with those of the literature with 7.2% of cases. However, this broad range of figures is essentially related to the time interval used to define permanent hypoparathyroidism, as this period can vary from 6 months to 2 years, while cases of recovery have been reported even after 2 years [11]. Nevertheless, although the symptoms related to permanent hypoparathyroidism may appear to be more acceptable in terms of the patient's quality of life than the voice and/or swallowing disorders related to recurrent laryngeal nerve paralysis, permanent hypoparathyroidism can be difficult to treat and may require life-long calcium and vitamin D supplements.

Value of level VI lymph node dissection

Central compartment (level VI) dissection is indicated in differentiated thyroid carcinoma of the follicular epithelium with the presence of level VI lymph nodes, especially when they are suspicious, demonstrated on imaging or intraoperatively.

Prophylactic central compartment dissection is systematically indicated in stage T2, T3 or T4 differentiated thyroid carcinoma of the follicular epithelium, based on T stage determined on frozen section examination or suspected preoperatively by positive fine-needle aspiration cytology and imaging (neck and chest ultrasound or CT).

In contrast, no consensus has been reached concerning the indications for prophylactic central compartment dissection in stage T1 N0 differentiated thyroid carcinoma of the follicular epithelium, particularly microcarcinomas (< 10 mm).

The essential question to be resolved is whether resection of lymph nodes with a normal appearance at thyroidectomy is clinically useful and whether it is associated with a favourable benefit/risk balance for the patient.

The rationale for prophylactic lymph node dissection is based on the suspicion of a high incidence of occult lymph node metastases, often microscopic, even in the context of papillary microcarcinoma [12]. However, the decision to perform prophylactic central compartment dissection cannot be justified exclusively on the discovery of subclinical lymph node metastases, but must be based on a demonstrated benefit for the patient, i.e. in terms of recurrence or survival. However, evidence in favour of a reduction of mortality following central compartment dissection has only been reported in two studies and remains controversial [13,14], as other studies have reported contradictory results [15—17].

Furthermore, the apparent discordance between the relatively high rate of occult lymph node metastases detected on prophylactic central compartment dissection and the relatively low recurrence rate after total thyroidectomy without lymph node dissection could be correlated with adjuvant radioiodine therapy.

In conclusion, arguments in favour of prophylactic central compartment dissection could be as follows:

- the high rate of cervical lymph node metastases, especially in papillary thyroid carcinoma (20 to 50% of cases); micrometastases appear to be even more frequent (up to 90% of cases) [3];
- preoperative and intraoperative findings are not always sufficient to confirm the diagnosis of lymph node metastases [18—20];
- systematic central compartment dissection associated with total thyroidectomy for thyroid carcinoma of the follicular epithelium does not increase the permanent complication rate of total thyroidectomy, in contrast with central compartment dissection performed secondarily after total thyroidectomy, which is associated with much higher morbidity [6,20—24];
- central compartment dissection allows precise staging of the cancer, allowing the patient to be classified as N0/N1, which is a major element to guide treatment, particularly for the indications for adjuvant radioiodine therapy [25,26];
- lymph node dissection would have a beneficial impact on ''subsequent events'', especially a lower local recurrence rate [10,15,16,20,27]. In contrast, the presence of lymph node metastases does not appear to alter survival, [15—17], except for patients over the age of 45 years [13,14,25,28].

Finally, the arguments against prophylactic central compartment dissection are essentially the absence of randomized prospective trials indicating the benefits of this surgery for patients with T1 N0 cancer in terms of improvement of the recurrence rate or survival. Furthermore, the published studies that reported a gain in terms of recurrence rate did not clearly distinguish between therapeutic and prophylactic lymph node dissections. There is therefore no formal evidence of the value of these procedures.

Conclusion

This study confirms the absence of any additional permanent morbidity of central compartment dissection associated with total thyroidectomy. This finding, together with demonstration of the extremely lymphophilic nature of thyroid carcinoma of the follicular epithelium (especially papillary cancers and even microcarcinomas), could encourage a more aggressive approach by proposing systematic prophylactic central compartment dissection whenever possible (positive frozen section examination demonstrating stage T1 papillary carcinoma). This approach may be justified to prevent local recurrence, although it does not appear to improve overall survival.

Although surgical morbidity must certainly be taken into account, the morbidity of radioiodine therapy although rare, must also not be ignored. Precise lymph node staging can therefore allow better selection of patients likely to benefit from adjuvant radioiodine therapy.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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